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## **Exhibit A**

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Re: Application Serial No. 09/781,182 filed February 12, 2001

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**Message:**

Dear Examiner Lewis,

Pursuant to your request earlier this afternoon, attached is a draft set of amended claims for purposes of our discussion next Tuesday (September 27, 2005) at 2 PM.

Please let me know if you should need any further information at this time. If not, I look forward to our discussion on Tuesday.

Sincerely,

Michael J. Ryan

Please call us immediately if the facsimile you receive is incomplete or illegible. Please ask for the facsimile operator.

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Application of: **VOURNAKIS *et al.***

Confirmation No.: **2779**

Serial No.: **09/781,182**

Art Unit: **1644**

Filed: **February 12, 2001**

Examiner: **P. T. Lewis, Ph.D.**

For: **COMPOSITIONS AND METHODS FOR  
MODULATION OF VASCULAR  
STRUCTURE AND/OR FUNCTION**

Attorney Docket No.: **7867-022-999**

**AMENDMENT AND REPLY UNDER 37 C.F.R. § 1.116**

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**Commissioner for Patents**

**P.O. Box 1450**

**Alexandria, VA 22313-1450**

**Sir:**

In response to the Office Action mailed January 24, 2005, (the "Office Action") Applicants respectfully request that the following remarks be considered by the Examiner and the following amendments be entered into the record of the above-captioned application. Applicants submit herewith an Amendment Fee Transmittal Sheet. A Petition for Extension of Time and a Notice of Appeal from the Primary Examiner to the Board of Patent Appeals and Interferences were filed on July 21, 2005.

**Amendments To The Claims begin on page 2 of this paper.**

**Remarks begin on page 6 of this paper.**

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-38 (Canceled)

39. (Currently amended) A method for achieving at least a transient, localized, modulation of vascular structure and/or function, comprising:

topically administering to a patient in need of said modulation, a sufficient amount of a ~~porous~~ non-barrier forming material comprising poly- $\beta$ -1 $\rightarrow$ 4 N-acetylglucosamine polymers, wherein the poly- $\beta$ -1 $\rightarrow$ 4 N-acetylglucosamine polymer comprises about 50 to about 150,000 N-acetylglucosamine monosaccharides covalently attached in a  $\beta$ -1 $\rightarrow$ 4 conformation, wherein the non-barrier forming material is in the form of a solution, a suspension, an emulsion, a spray, or a foam, so that the patient experiences at least a transient, localized modulation of vascular structure and/or function.

40. (Previously presented) The method of claim 39, wherein the method achieves at least a transient, localized physiological response comprising stimulation of endothelin-1 release.

41. (Previously presented) The method of claim 40, wherein the endothelin-1 is released from vascular endothelial cells.

42. (Previously presented) The method of claim 39, wherein the method achieves at least a transient, localized physiological response comprising vasoconstriction.

43. (Previously presented) The method of claim 39, wherein the method achieves at least a transient, localized physiological response comprising reduction in blood flow out of a breached vessel.

44. (Previously presented) The method of claim 43, wherein the patient experiences cessation of blood flow out of the breached vessel.

45. **(Previously presented)** The method of claim 39, wherein the poly- $\beta$ -1 $\rightarrow$ 4 N-acetylglucosamine polymer comprises about 50 to about 50,000 N-acetylglucosamine monosaccharides covalently attached in a  $\beta$ -1 $\rightarrow$ 4 conformation.
46. **(Previously presented)** The method of claim 45, wherein the poly- $\beta$ -1 $\rightarrow$ 4 N-acetylglucosamine polymer comprises about 50 to about 10,000 N-acetylglucosamine monosaccharides covalently attached in a  $\beta$ -1 $\rightarrow$ 4 conformation.
47. **(Previously presented)** The method of claim 46, wherein the poly- $\beta$ -1 $\rightarrow$ 4 N-acetylglucosamine polymer comprises about 50 to about 4,000 N-acetylglucosamine monosaccharides covalently attached in a  $\beta$ -1 $\rightarrow$ 4 conformation.
48. **(Previously presented)** The method of claim 39, wherein the poly- $\beta$ -1 $\rightarrow$ 4 N-acetylglucosamine polymer comprises at least one non-acetylated glucosamine monosaccharide unit, and wherein at least 40% of the glucosamine monosaccharide units are N-acetylated.
49. **(Previously presented)** The method of claim 39, wherein the patient is a human.
50. **(Canceled)**
51. **(Currently amended)** The method of claim 39, wherein the ~~porous~~ non-barrier forming material is applied directly to a blood vessel.
52. **(Previously presented)** The method of claim 39, wherein the vascular structure is a blood vessel selected from the group consisting of capillary, vein, and artery.
53. **(Previously presented)** The method of claim 52, wherein the blood vessel is a breached blood vessel.
54. **(Previously presented)** The method of claim 53, whereby the patient experiences cessation of bleeding.

55. **(Previously presented)** The method of claim 39, wherein the extent of the transient, localized modulation of vascular structure and/or function is substantially proportional to the amount of poly- $\beta$ -1 $\rightarrow$ 4 N-acetylglucosamine administered.

56. **(Previously presented)** The method of claim 39, wherein said polymers are substantially free of protein.

57. **(Previously presented)** The method of claim 39, wherein said polymers are substantially free of organic contaminants.

58. **(Previously presented)** The method of claim 39, wherein said polymers are substantially free of inorganic contaminants.

59. **(Currently amended)** A method for treating a patient having a vascular disorder, comprising:

topically administering to a patient in need of such treatment, a sufficient amount of a porous non-barrier forming material comprising poly- $\beta$ -1 $\rightarrow$ 4 N-acetylglucosamine polymers, wherein the poly- $\beta$ -1 $\rightarrow$ 4 N-acetylglucosamine polymer comprises about 50 to about 150,000 N-acetylglucosamine monosaccharides covalently attached in a  $\beta$ -1 $\rightarrow$ 4 conformation, wherein the non-barrier forming material is in the form of a solution, suspension, emulsion, spray, or foam, whereby said administering ameliorates said vascular disorder.

60. **(Previously presented)** The method of claim 59, wherein the vascular disorder is selected from the group consisting of menorrhagia, cerebral aneurysm, abdominal aneurysm, uterine fibroid lesion, and blood vessel puncture.

61. **(Previously presented)** The method of claim 59, wherein said polymers are substantially free of protein.

62. **(Previously presented)** The method of claim 59, wherein said polymers are substantially free of organic contaminants.

63. **(Previously presented)** The method of claim 59, wherein said polymers are substantially free of inorganic contaminants.

64. **(Previously presented)** The method of claim 59, wherein the method achieves at least a transient, localized physiological response comprising stimulation of endothelin-1 release.

65. **(Previously presented)** The method of claim 59, wherein the method achieves at least a transient, localized physiological response comprising vasoconstriction.

66. **(Previously presented)** The method of claim 59, wherein the method achieves at least a transient, localized physiological response comprising reduction in blood flow out of a breached vessel.